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Echo-Spacing Optimization for the Simultaneous Measurement of Reversible (R_2') and Irreversible (R_2) Transverse Relaxation Rates

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Abstract

Accurate measurement of reversible (R_2') and irreversible (R_2) transverse relaxation rates plays a key role in various MRI research and applications. Although optimizing the echo spacing for a multi-echo pulse sequence measuring a single exponential decay has been investigated, optimization in sequences such as GESFIDE (Gradient-Echo Sampling of Free Induction Decay and Echo), in which two echo trains are simultaneously measured to obtain both R_2 and R_2' , has not been reported. In this work, optimum echo spacings for the GESFIDE sequence are determined to improve the accuracy of the measured relaxation parameters. Various relaxation rates and numbers of acquired echoes are considered, as well as whether or not the receiver bandwidth is kept fixed or varied with the echo spacing. In the case of constant receiver bandwidth, results show that the echo train length approximately equal to T_2^* should be used for each echo train in GESFIDE to minimize the uncertainty in R_2 or R_2' . If the receiver bandwidth is allowed to change with echo spacing in order to maximize the image SNR, the optimum echo train length will vary, generally increasing with the number of echoes.

Keywords

Magnetic Resonance Imaging (MRI); echo spacing; transverse relaxation rates; GESFIDE; gradient echo; spin echo

1. Introduction

Accurate measurement of transverse relaxation rates, including irreversible (R_2), reversible (R_2'), and total (R_2^*) relaxation rates (or their inverses, the transverse relaxation times T_2 , T_2' , and T_2^* respectively) are important and of extensive interest in many areas of MR research, including studies that involve brain iron [1,2], integrity of trabecular bone [3,4], iron-overloading diseases [5,6] and gel dosimetry [7,8]. Although R_2^* or R_2 could each be measured in a single scan with multiple gradient or spin echo sequences, respectively, R_2' typically requires multiple acquisitions [5]. A means to measure both R_2 and R_2' (as well as R_2^*) in a single scan was previously reported [9]. The GESFIDE (Gradient-Echo Sampling of Free Induction Decay and Echo) sequence, shown in Fig. 1, consists of two echo trains, one immediately following the excitation pulse, and a second following the 180° refocusing pulse.

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The signal in the first train of gradient echoes decays exponentially with a rate constant R_2^* ($= R_2 + R_2'$), while in the second the signal evolves with a rate constant R_2^- ($= R_2 - R_2'$). Following the calculation of R_2^* and R_2^- , R_2 and R_2' could be computed from their linear combinations.

Some efforts have been made to optimize the R_2 measurement accuracy for single exponential decay pulse sequences such as the multiple spin echo sequence. In a study of polymer gel dosimetry, the echo spacing and the total number of echoes were experimentally found to be parameters of particular importance in minimizing the uncertainty in T_2 [7]. Unequal echo spacings have also been suggested and examined to improve R_2 measurement accuracy for multi-spin echo pulse sequences [10,11].

In this paper, the relaxation rate measurement uncertainty was first analyzed for single exponential decay pulse sequences to lay the initial framework. Optimum echo spacings were determined for the cases of both constant and variable receiver bandwidths. The analysis was then extended to GESFIDE, in which the optimum echo spacing was simultaneously optimized numerically for the two echo trains. The measurement uncertainty in R_2 and R_2' as a function of the echo spacing, the number of echoes acquired, and the relaxation rates were systemically studied and the results were compared with those of the single decay analysis. For practical reasons as well as for generalizability, only equal echo spacing was considered in this study.

2. Theory and Methods

2.1 Standard Multi-Echo Pulse Sequences

A fit to an R_2^* decay from a multiple-echo gradient echo (GRE) pulse sequence will be considered, but the results could also be applied to a multiple spin echo sequence by simply replacing R_2^* with R_2 (ignoring effects of imperfect RF and stimulated echoes). In the GRE pulse sequence, the decaying signal could be expressed as $S_n = S_1 \exp[-(n-1)\tau R_2^*]$ where τ is the echo spacing, S_1 is the signal at the first echo, and $n = 1, 2, 3, \dots, N$, where N is the total number of echoes. Assuming that the noise in each image has the standard deviation σ , R_2^* could be computed as the slope determined from a linear least squares regression of $\log(S_n)$ vs. $n\tau$ with an appropriate weighting factor,

$$w_n = (S_n / \sigma)^2 \quad (1)$$

The R_2^* measurement uncertainty can be expressed as follows [12,13]:

$$\sigma_{R_2^*} = \sqrt{\sum w_n / (\sum w_n \sum w_n n^2 \tau^2 - [\sum w_n n \tau]^2)} \quad (2)$$

2.1.1 Constant receiver bandwidth—If the readout time for each echo (and hence the receiver bandwidth) is kept constant, the noises remain independent of the echo spacing, and then are the same for all images. The R_2^* measurement uncertainty in Eq.(2) could be analyzed by examining its dependence on three parameters: R_2^* , τ and the number of echoes N . However, the analysis could be simplified by introducing a dimensionless parameter, η , defined as the ratio of the time between the first and last echoes (“echo train length”) to the relaxation time T_2^* ($\eta = (N-1) \tau R_2^*$). Eq.(2) could then be expressed as

$$\sigma_{R_2^*}^{CB} = \frac{R_2^*}{SNR_1} u^{CB}(N, \eta) \quad (3)$$

where $u^{CB}(N, \eta)$ is a normalized measurement uncertainty for the case of constant bandwidth

$$u^{CB}(N, \eta) = \frac{(N-1)}{\eta} \sqrt{\sum S_{n\eta}^{CB} / (\sum S_{n\eta}^{CB} \sum S_{n\eta}^{CB} n^2 - [\sum S_{n\eta}^{CB} n]^2)} \quad (4)$$

$$S_{n\eta}^{CB} = \exp[-2n\eta / (N-1)] \quad (5)$$

and $SNR_1 = S_1/\sigma$ is the SNR of the first echo. In this manner, the R_2^* and the image SNR is effectively separated from $u^{CB}(N, \eta)$, which is only a function of N and η . The uncertainty, $\sigma_{R_2^*}^{CB}$ for various R_2^* values and image SNR could then be analyzed by simply examining $u^{CB}(N, \eta)$. The optimum value of η , η_0 , at which $u^{CB}(N, \eta)$ is minimized for a given N , could be determined by solving $\partial u^{CB}(N, \eta) / \partial \eta = 0$. The optimum echo spacing, τ_0 , could subsequently be computed from η_0 , and the R_2^* measurement uncertainty determined according to Eq.(3).

2.1.2 Variable receiver bandwidth—With larger echo spacings, reduced receiver bandwidths could be used to increase image SNR. The noise standard deviation, σ could then be approximated by a function of echo spacing: $\sigma = \sigma_{nom} \sqrt{\tau_{nom} / \tau}$, where τ_{nom} (assumed to be 1.5 ms in this study) and σ_{nom} are nominal echo spacing and noise standard deviation, respectively. By simple substitutions into the above equations, the uncertainty for variable bandwidth could be expressed as

$$\sigma_{R_2^*}^{VB} = \frac{R_2^{*3/2} \tau_{nom}^{1/2}}{SNR_{nom}} u^{VB}(N, \eta) \quad (6)$$

where SNR_{nom} is the SNR of the first echo when $\tau = \tau_{nom}$ and

$$u^{VB}(N, \eta) = \left(\frac{N-1}{\eta} \right)^{3/2} \sqrt{\sum S_{n\eta}^{VB} / (\sum S_{n\eta}^{VB} \sum S_{n\eta}^{VB} (n+1/2)^2 - [\sum S_{n\eta}^{VB} (n+1/2)]^2)} \quad (7)$$

where $S_{n\eta}^{VB} = \exp[-(2n+1)\eta / (N-1)]$. In the above equations, we make the simple assumption that the first echo time also varies with the echo spacing as $\tau/2$. As above, the analysis of R_2^* measurement uncertainty is simplified by examining $u^{VB}(N, \eta)$, and the corresponding optimum η_0 and τ_0 , could be determined from $\partial u^{VB}(N, \eta) / \partial \eta = 0$.

2. 2 The GESFIDE pulse sequence

In GESFIDE, R_2 and R_2' are calculated from the computed relaxation rates R_2^* and R_2^- (Fig. 1): $R_2 = (R_2^* + R_2^-)/2$ and $R_2' = (R_2^* - R_2^-)/2$. Thus the measurement uncertainty for both R_2 and R_2' could be expressed as

$$\sigma_{R_2} = \sigma_{R_2'} = \sqrt{\sigma_{R_2^*}^2 + \sigma_{R_2^-}^2} / 2 \quad (8)$$

The optimization of GESFIDE for R_2 and R_2' measurement accuracies is more complicated compared to a single exponential pulse sequence. In order to minimize the R_2 measurement uncertainty, the R_2^* measurement uncertainty needs to be reduced, while at the same time, adequate signal should be preserved for the second echo train to diminish the R_2^- measurement uncertainty.

It is assumed that the echo spacings and the number of echoes, N , for both echo trains are identical in our analysis since the times available for the two echo trains are approximately equal. For the case of constant bandwidth the R_2^* measurement uncertainty $\sigma_{R_2^*}^{CB}$ could be expressed as shown in Eqs. (3) and (4), and $\sigma_{R_2^-}^{CB}$ could also be represented by Eqs.(3) and (4)

simply by replacing R_2^* with R_2^- and SNR_1 with that of the first image of the second echo train:

$$\sigma_{R2-}^{CB} = \frac{R_2^* \beta}{SNR_1} \exp \left\{ \eta + R_2^* T_p (1 + \beta) / 2 \right\} u^{CB}(N, \beta \eta) \quad (9)$$

where $\beta = R_2^-/R_2^*$ and T_p (assumed 5 ms in this work, but the analysis should be valid for other values of T_p as long as $T_p \ll (N-1)\tau$) is the separation between the last echo of the first echo train and the first echo of the second echo train as shown in Fig. 1. It should be pointed out that R_2^- could be either positive or negative and β ranges from -1 to $+1$, depending on the relative values of R_2 and R_2' . In Eq. (9), it is also assumed that the 180° refocusing pulse is at the center of T_p , a valid assumption as long as the first echo time is small relative to the length of the echo train.

Combining Eqs. (3), (8) and (9) we obtain

$$\sigma_{R2}^{CB} = \frac{R_2^*}{2SNR_1} u_{R2}^{CB}(N, \eta, R_2^*) \quad (10)$$

where the normalized R_2 measurement uncertainty for GESFIDE is

$$u_{R2}^{CB}(N, \eta, R_2^*) = \left\{ u^{CB}(N, \eta)^2 + \exp[2\eta + T_p R_2^* (1 + \beta)] \beta^2 u^{CB}(N, \beta \eta)^2 \right\}^{1/2} \quad (11)$$

The above equations show a dependence of u_{R2}^{CB} on the relaxation rate R_2^* . However, this dependence is minimal since $T_p(1+\beta)$ is typically much smaller than the total length of the echo trains, $2(N-1)\tau$.

For the case of variable receiver bandwidth, the R_2 measurement uncertainty, σ_{R2}^{VB} , could similarly be derived as

$$\sigma_{R2}^{VB} = \frac{R_2^*{}^{3/2} \tau_{\text{nom}}^{1/2}}{SNR_{\text{nom}}} u_{R2}^{VB}(N, \eta, R_2^*) \quad (12)$$

where

$$u_{R2}^{VB}(N, \eta, R_2^*) = \left\{ u^{VB}(N, \eta)^2 + \exp[2\eta + \eta \frac{(1+\beta)}{N-1} + T_p R_2^* (1 + \beta)] |\beta|^3 u^{VB}(N, \beta \eta)^2 \right\}^{1/2} \quad (13)$$

For the standard multi-echo pulse sequence, the optimum lengths of the echo trains were determined by numerically solving the equations $\partial u^{CB}/\partial \eta = 0$ and $\partial u^{VB}/\partial \eta = 0$ for constant and variable receiver bandwidths, respectively. For GESFIDE, η_0 was obtained by numerically minimizing $u_{R2}^{CB}(N, \eta, R_2^*)$ and $u_{R2}^{VB}(N, \eta, R_2^*)$, respectively, as functions of the three parameters. All processing was performed in IDL (Interactive Data Language, Research System, Inc, Boulder, Co).

3. Results and Discussion

3.1 Standard Multi-Echo Pulse Sequences

Fig. 2 shows the relationship between η_0 ($= (N-1)\tau_0 R_2^*$), at which $u^{CB}(N, \eta)$ or $u^{VB}(N, \eta)$ are minimized, and the number of acquired echoes N . In the case of constant receiver bandwidth (solid squares), η_0 is approximately equal to 2 for $N = 4$, indicating that for a multi-gradient

echo sequence using fixed receiver bandwidth, the echo train length should be approximately twice the relaxation time T_2^* (or T_2 for a spin-echo sequence). This result is in good agreement with previous observations in experimental data in gels [7]. In the case where the receiver bandwidth is allowed to change with echo spacing (solid circles), η_0 increases with N without an apparent plateau in the range investigated. Although the receiver bandwidth actually increases with N , higher η_0 permits the rate of this increase to be smaller (minimizing reduction in SNR) than if a plateau had existed.

Fig. 3 presents a plot of $u^{VB}(N, \eta)$ vs. η for various values of N for the case of variable bandwidth. It could be seen from the figure that the plots become flatter with increasing N , indicating that an exact value of η_0 may be less critical with increasing number of echoes. Since the plots are relatively flat between the optimum points (triangles) and the point where $\eta = 2$, $\eta = 2$ may be prescribed for up to 10 echoes, the range that is typically used in MRI, although larger η may be desired for $N > 10$. The maximum deviation, $[u^{VB}(10, 2) - u^{VB}(10, \eta_0)]/u^{VB}(10, \eta_0)$, is less than 11% in this range of N .

The reduction in R_2^* measurement uncertainty with increasing number of echoes could be investigated by plotting $u^{CB}(N, \eta_0)$ and $u^{VB}(N, \eta_0)$ with respect to N as shown in Fig. 4. The values of $u^{CB}(N, \eta_0)$ and $u^{VB}(N, \eta_0)$ were normalized to 1 at $N = 3$ by factors of 2.3 and 4.6, respectively. The R_2^* measurement uncertainty could then be obtained from Eqs. (3) and (6), combined with the results in Fig. 4, adjusted by the corresponding normalized factors. For both constant and variable bandwidths, the rate of improvement in R_2^* accuracy with increasing N is initially high for small N , and declines with higher N . For the case of constant bandwidth a plateau is not observed, but the curve for the variable bandwidth shows approximately leveling off near $N = 10$. For the latter, the fractional improvements that could be achieved with 30 echoes, as compared to 3, 5, and 10 echoes are, respectively, $u^{VB}(3, \eta_0)/u^{VB}(30, \eta_0) = 1.8$, $u^{VB}(5, \eta_0)/u^{VB}(30, \eta_0) = 1.4$, and $u^{VB}(10, \eta_0)/u^{VB}(30, \eta_0) = 1.15$.

3.2 The GESFIDE pulse sequence

For GESFIDE, the analysis is more complicated as R_2 measurement uncertainty and η_0 both depend on N , R_2^* and β . Fig. 5 illustrates the variation of η_0 with β for several values of R_2^* and $N = 7$ for both constant and variable receiver bandwidths. η_0 decreases with increasing β due to that fact that for a given R_2^* , larger β indicates signal evolution increasingly dominated by irreversible signal decay (losses due to R_2), and thus shorter echo spacings are favored. Compared to the case of the standard multi-echo pulse sequence where η_0 is independent of R_2^* , it is interesting to note that, for a given β , η_0 for GESFIDE is also not strongly dependent on R_2^* . In other words, the optimum length of echo train in GESFIDE depends primarily on the ratio of the post- and pre-180 decay rates. The weak R_2^* -dependence of η_0 is also observed for other values of N .

The variations in η_0 as a function of β for various N are illustrated in Fig. 6. The curves were generated using $R_2^* = 50/\text{sec}$, but are representative for other values as well due to the weak R_2^* dependence of η_0 as demonstrated in Fig. 5. The figure shows that the optimum echo train length decreases and converges for all N with increasing β , presumably due to higher irreversible signal decay, concomitantly reducing the available data acquisition period.

Figure 7 shows the plots of $u_{R_2}^{CB}(N, \eta, R_2^*)$ and $u_{R_2}^{VB}(N, \eta, R_2^*)$ as a function of for $R_2^* = 50/\text{sec}$, $N = 5$, and various values of β . The figure demonstrates that a single value of $\eta = 1$ is a good approximation to minimize the measurement uncertainty for the case of constant receiver bandwidth, although the actual optimum η could differ by a factor of 2 according to Fig. 5. The additional error due to the utilization of $\eta = 1$ rather than the optimum η_0 , $[u_{R_2}^{CB}(N, 1, R_2^*) - u_{R_2}^{CB}(N, \eta_0, R_2^*)]/[u_{R_2}^{CB}(N, \eta_0, R_2^*)]$, were examined for $R_2^* = 20/\text{sec}$ –

250/sec and $N = 4 - 10$ (a range that would likely be used in practice), and it was found that the maximum additional uncertainty is approximately 16%. For the case of the variable receiver bandwidth, however, the maximum additional uncertainty for the same range of parameters is approximately 35%.

The above results did not take into account the various factors that could limit the minimum achievable echo spacing, such as maximum gradient amplitudes and slew rates, and RF pulse durations for spin echo sequences. Furthermore, the maximum desired readout time could be determined by other factors, such as chemical shift or field inhomogeneity effects. If the minimum possible echo spacing $\tau_{\min}$ for a given bandwidth exceeds the optimum spacing τ_0 (for constant bandwidth), then $\tau_{\min}$ should be prescribed to ensure the best measurement accuracy. If the bandwidth, however, is allowed to change, then τ_0 for the variable bandwidth should be used, while using the maximum possible readout time.

In summary, the optimization of echo spacing for the measurement of transverse relaxation parameters has been systematically examined. For the case of constant bandwidth, the optimum total data acquisition period for each echo train is approximately twice the transverse relaxation time in sequences that measure single exponential decays (multi-gradient or spin echo), while the optimum for each echo train in GESFIDE is approximately equal to T_2^* . If the receiver bandwidth is allowed to vary with echo spacing, the optimum acquisition period will vary, generally increasing with the number of acquired echoes. These findings provide a general guideline to design pulse sequences for the optimization of transverse relaxation rate measurements.

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Fig. 1.

The GESFIDE pulse sequence consists of two trains of gradient-echoes: The first train samples the signal decaying with rate constant R_2^* after initial excitation. The second train samples the signal evolving with rate constant R_2^- following the refocusing pulse. Parameters of interest (R_2 and R_2') can be directly computed from the sum and difference of R_2^* and R_2^- .

Fig. 2. The optimum ratio of the echo train length to T_2^* [$\eta_0 = (N-1)t_0/T_2^*$] as a function of number of echoes acquired, N , for the cases of constant bandwidth (solid squares) and variable bandwidth (solid circles).

Fig. 3.

The normalized R_2^* measurement error, $u^{VB}(N, \eta)$, as a function of η ($\eta = (N-1) \tau/T_2^*$) for the case of variable bandwidth. $\eta = 2$ could be selected as an approximate optimal point with little additional error for N up to 10, although the exact optimal points (triangles) may be substantially different.

Fig. 4.

The dependence of optimal normalized measurement uncertainty $u^{CB}(N, \eta_0)$ (constant bandwidth) and $u^{VB}(N, \eta_0)$ (variable bandwidth) on N . The values of $u^{CB}(N, \eta_0)$ and $u^{VB}(N, \eta_0)$ are normalized to 1 at $N = 3$ by normalized factors of 2.3 and 4.6, respectively. The R_2^* measurement accuracy is considerably improved with the increases of N initially, then the rate of improvement declines and plateaus at approximately $N = 10$ for the case of variable receiver bandwidth. However, the uncertainty continues to decrease for the constant receiver bandwidth.

Fig. 5.

A plot of η_0 vs. β ($= R_2^-/R_2^*$) for $N = 7$ for a set of R_2^* in the cases of variable bandwidth (top lines) and constant bandwidth (bottom lines). For a given β , η_0 varies only slightly for different R_2^* .

Fig. 6a

Fig. 6b

Fig. 6. A plot of η_0 vs. β in the cases of constant (Fig. 6a) and variable (Fig. 6b) bandwidths. η_0 is approximately independent of N for higher β .

Fig. 7a

Fig. 7b

Fig. 7. Plots of the measurement uncertainty as a function of η for different β ($N = 5$, $R_2^* = 50/\text{sec}$) for constant (Fig. 7a) and variable (Fig. 7b) bandwidths.